

4-18634\A\CONT2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
YIQING ZHOU ET AL.
SERIAL NO.: 08/216,440
FILED: MARCH 23, 1994
FOR: ANTIMALARIAL COMPOSITIONS

Commissioner of Patents and Trademarks
Washington D.C. 20 231 USA

DECLARATION UNDER RULE 132

Sir:

I, the undersigned, Yiqing Zhou, citizen of China, resident of Beijing, do hereby depose and declare as follows:

That I am a graduate of The Second Military University of Shanghai, China, where I graduated in July 1960;

That I am now a professor of malaria research;

That I am the author of 4 publications in the field of antimalaria research;

That I am a member of the following professional organisation: The Chinese Society of Pharmacology;

That I am presently working in the Division of Research and Development of Antimalarial Agents at the Academy of Military Medical Sciences, Beijing, China;

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That I am a co-inventor of this application;

That upon my request and under my guidance clinical experimental studies on the activity of the antimalarial agents artemether, benflumetol, and chloroquine have been performed in 1988 in endemic areas of chloroquine resistance in Hainan Island, China, and that I have checked for adequacy and correctness the data obtained from those tests;

That the results obtained from said studies and the conclusions drawn therefrom are the following:

1. Materials and Methods

1.1. Artemether group

The artemether injection formulation for intramuscular administration is provided by Kun Ming pharmaceutical factory, China.

The treatment regimen extends up to five days for each adult. The mode of administration is by intramuscular injection. The dose of artemether administered is 160 mg on the first day and 80 mg on each subsequent day. The total dose administered is 480 mg.

1.2. Benflumetol group

The treatment regimen extends up to six days for each adult. Benflumetol is administered orally three times daily in the form of a capsule formulation containing an oily suspension of 200 mg of the active agent. The total dose administered is 3.6 g.

1.3. Artemether and benflumetol group

The treatment regimen extends up to four days for each adult.

The artemether is administered three times by intramuscular injection of a dose of 80 mg for each administration at 0, 24, and 48 hours. The total dose of artemether administered is 240 mg. Benflumetol is administered orally three times daily in the form of a capsule formulation containing an oily suspension of 200 mg of the active agent. The total dose administered is 2.4 g.

1.4 Chloroquine group

Chloroquine tablets are administered orally according to the standard method prescribed by WHO, the total dose of administration is 1.5 g.

2. Results

The results are shown in the following Table:

Group	Cases	Parasite Clearance Time (h)	Fever Subsidence Time (h)	Cure Rate 28 th Day
Artemether inj. 1.1	20	71.5 ± 15.1	22.3 ± 13.5	87.2
Benflum. Caps. 1.2	20	72.1 ± 19.8	42.0 ± 20.2	96.5
Artem./Benflum. 1.3	20	40.1 ± 9.6	23.6 ± 6.2	92.5
Chloroquine 1.4	20	87.3 ± 24.7	56.5 ± 23.7	40.9

The Undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issueing thereon.

Signed at Beijing, China this 4 day of August 1994



Professor Yiqing Zhou